Annals of Clinical and Analytical Medicine
Original Research

An investigation of procalcitonin/albumin ratio as a predictor of mortality in patients with sepsis

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Abstract

Aim: Sepsis is a condition that results in mortality as a result of multiorgan failure associated with infection. Therefore, a number of parameters are used to determine the prognosis of sepsis. Accordingly, the ratio of procalcitonin and albumin found recent use for the above purpose. The present study aimed to investigate the value of the procalcitonin/albumin ratio to determine the prognosis of sepsis patients.

Material and Methods: The present study was designed as a single-center, prospective research. The study included patients admitted to the intensive care unit upon diagnosed with pneumosepsis and met the inclusion criteria. Patients with pneumonic infiltration in the lungs supported by computed tomography images and a qSOFA score≥2 were considered to have pneumosepsis.

Results: The present study included 299 patients, who were admitted to the intensive care unit upon pneumosepsis diagnosis. The procalcitonin/albumin ratio in the mortality group and survivors was 0.42 and 0.004, respectively. The sensitivity and specificity for mortality were 87.4% and 77.6%, respectively, for a cut-off value of 0.010 for the procalcitonin/albumin ratio.

Discussion: The results of the present study were indicative of the fact that elevated procalcitonin/albumin ratio was significant in predicting prognosis in patients, who were admitted to the intensive care unit upon pneumosepsis diagnosis. This suggested that procalcitonin/albumin ratio might serve as a prognostic indicator on the grounds that the severity of sepsis was associated with the change in acute phase reactants.

Keywords

Sepsis, Procalcitonin/Albumin Ratio, Mortality, Acute Phase Reactants

DOI: 10.4328/ACAM.22203 Received: 2024-03-28 Accepted: 2024-05-20 Published Online: 2024-05-25 Printed: 2024-06-01 Ann Clin Anal Med 2024;15(6):444-448
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This study was approved by the Ethics Committee of Basaksehir Cam and Sakura City Hospital (Date: 2021-12-29, No: 2021.12.304)

Introduction

Sepsis is a clinical condition characterized by excessive release of inflammatory mediators and cytokines as induced by the uncontrolled response of the host against infection, which may lead to life-threatening organ dysfunction, specifically involving the heart and kidneys. There has been an increase in the incidence of sepsis especially in recent years [1]. In the US, approximately 3% of patients, who are admitted to hospital, are diagnosed with sepsis. The focus is pneumonia in most patients diagnosed with sepsis. Half of such patients would require admission to the intensive care unit (ICU) [2]. The outcome of the majority of pneumosepsis patients, who are admitted to the ICU, is mortality. Furthermore, the cost of sepsis treatment increases each day due to the prolonged treatment process [2]. Procalcitonin (PCT) is a peptide produced in thyroid C cells and adipose tissue [3]. While it is at a low level under physiologic conditions, serum PCT level increases upon production by a number of tissues especially in case of systematic inflammation, including bacterial infection [4]. In addition, PCT levels increase in certain noninflammatory conditions, such as shock, trauma, surgery, burns, and chronic renal failure (CRF) [4]. Recently, PCT has been adopted as a biomarker by clinicians in the diagnosis of sepsis [5]. Albumin (ALB) is a protein synthesized by liver hepatocytes and considered the most abundant protein in circulation. Despite the fact that ALB is generally used as an indicator of nutrition, ALB levels also decrease in cases of excessive alcohol intake, cirrhosis, hepatitis, and liver failure [6, 7]. Previous studies recently suggested that ALB was an indicator of inflammation due to the occurrence of hypoalbuminemia in case of inflammation [8].

The PCT/ALB ratio (PAR) is a parameter calculated by dividing the PCT level by the ALB level. This parameter is indicative of both the inflammatory state of the body and the nutritional status. Recent studies demonstrated that PAR was a marker of poor prognosis in patients with sepsis [9]. Another study reported that PAR contributed to the determination of prognosis in sepsis [10]. Accordingly, PAR can be used as a quick, easy and simple marker of sepsis to reduce costs incurred by the healthcare system.

It is critical that prognosis is determined rapidly and accurately in patients, who have been diagnosed with sepsis. Therefore, the present study aimed to identify a reliable predictive biomarker to effectively assess the prognosis in patients with sepsis and to rapidly diagnose those patients and start their treatment earlier.

Material and Methods

Study design

This study was designed as a retrospective and single-center research. The study included patients, who were admitted to the respiratory ICU upon diagnosis with pneumosepsis. Patients with pneumonic infiltration and ground-glass appearance on thoracic computed tomography and who met the qSOFA (abnormal state of consciousness, respiratory rate ≥22/min, and systolic blood pressure ≤100 mmHg) criteria used for the diagnosis of sepsis in the surviving sepsis campaign: 2021 [11] guidelines were included in the study. Demographic characteristics, laboratory results, PCT, ALB, and PAR values as well as 28-day mortality status were captured on the case form.

Setting and selection of participants

The study included patients, who were admitted to the respiratory ICU with a diagnosis of pneumonia and had qSOFA scores of ≥2 points. Patients, who met the following criteria were excluded from the study:

- under 18 years of age,
- pregnant,
- incomplete patient data,
- history of malignancy,
- history of hematologic disease,
- bone marrow pathology,
- use of anti-inflammatory or immunosuppressive drugs,
- history of liver failure and cirrhosis,
- trauma patient,
- burn patient,
- history of CRF,
- history of surgery within the last 6 months,
- qSOFA score of <2 points. Patients diagnosed with pneumosepsis and not falling in the above criteria were included in the study

Eligible patients were identified upon review of the automation system [Hospital Information Management System (HIMS)]. All the patients, who were admitted to the respiratory ICU in the last 2 years, were included in the analyses. There were 423 patients with sepsis upon HIMS review. Of the 423 patients, 35 had a history of CRF, 22 had incomplete data, 21 had a qSOFA score of <2, 18 had a history of malignancy, 17 had liver failure or cirrhosis, 6 had a history of surgery, and 5 had a history of hematologic disease, and therefore excluded from the study. The remaining 299 patients were included in the study (Figure 1).

Demographic characteristics (age, sex) and clinical data (vital signs, laboratory values, outcomes and PCT, ALB, PAR ratio) of the patients included in the study were captured. For the clinical data of the patients, the values at admission were captured.

Data calculation

Calculations were made based on the results from the cases in the study. Accordingly, the neutrophil-to-lymphocyte ratio (NLR) and PAR ratios were calculated. The formulas were as follows: NLR = Neutrophil/Lymphocyte ratio and PAR = Procalcitonin/Albumin ratio. Due to the retrospective design of the study, the endpoints (discharge, exitus) during hospitalization were assessed.

Statistical analysis

The Statistical Package for the Social Sciences software, Version 24.0 was used for data analyses. Numbers, percentage, mean, standard deviation, median, median, minimum, and maximum values were used for the presentation of descriptive data. The Kolmogorov-Smirnov test was used to see if the hypothesis of normal distribution of the data was met. The continuous variables without normal distribution upon univariate analysis were expressed as median (IQR) and compared using the Mann–Whitney U test. The Pearson Chi-Squared test was used to analyze the categorical variables. Fisher's Exact test was used when there were <5 categorical variables. The receiver operating characteristic (ROC) curve analysis was used for diagnostic accuracy purposes; and further, sensitivity,

specificity, and area under the curve were calculated and the results presented.

A p-value of <0.05 was considered statistically significant.

Ethical Approval

The study was approved by the Ethics Committee of Basaksehir Cam and Sakura City Hospital (Date: 2021-12-29, No: 2021.12.304).

Table 1. An analysis of demographic data, vital parameters, and laboratory data of the cases

Parameter		
Age (years) Median (IQR)		66.0 (57.0–76.0)
Sex	Male	161 (53.8)
	Woman	138 (46.2)
Vital Parameters Median (IQR)	SBP (mmHg)	125.0 (105.0–144.0)
	DBP (mmHg)	70.0 (60.0–80.0)
	Pulse rate (beats/min)	95.0 (80.0-–110.0)
	Temperature (°C)	36.5 (36.4–36.6)
	Saturation (%)	95.0 (90.0–98.0)
	Respiratory Rate (/min)	24.0 (20.0–28.0)
Outcome (n (%))	Discharged	125 (41.8)
	Mortality	174 (58.2)

SBP: Systolic Blood Pressure (mmHg)
DBP: Diastolic Blood Pressure

Results

The study included 299 cases. 53.8% (n = 161) of the patients were men and 46.2% (n = 138) were women. The median age of the patients was 66 (57.0–76.0) years. As regards the endpoints, 41.8% of the patients were discharged, where the rate of mortality was 58.2%. The median length of hospital stays of the patients was 6 (3–18) days. The IQR values of the vital parameters from the patients included in the study are given in Table 1. Age, length of hospital stays, and vital and laboratory values were analyzed vis-à-vis the endpoints. Based on the study data, the median age was significantly higher in nonsurvivors. The systolic blood pressure, diastolic blood pressure, and saturation were significantly lower in nonsurvivors compared to survivors in terms of vital parameters. There were no differences in pulse rate, temperature, and respiratory rate by the outcome. The length of hospital stays was significantly higher in nonsurvivors (Table 2).

As regards the laboratory results, the lymphocyte values were significantly higher in the survivor patients, while there was no significant difference in white blood cell, neutrophil, and platelet values. Furthermore, the median procalcitonin value was significantly higher and the median albumin value was significantly lower in nonsurvivors compared to survivors (Table 2).

The median values of the PAR calculated by outcome were compared and accordingly these values were statistically

Table 2. A comparison of demographic data, vital parameters, and laboratory data by the outcome of the cases

Parameter		Outcome		p
		Exitus n (%)/ Median (IQR)	Survivor n (%)/ Median (IQR)	
Age (years)		69.5 (79.0–59.0)	62.0 (55.0–71.0)	<0.001
Vital Parameters	SBP (mmHg)	120.0 (100.0–135.0)	130.0 (116.0–150.0)	<0.001
	DBP (mmHg)	70.0 (60.0–80.0)	73.0 (5.0–80.0)	0.031
	Pulse rate (beats/min)	96.0 (79.0–112.0)	94.0 (80.0–107.0)	0.762
	Temperature (°C)	36.5 (36.4–36.6)	36.5 (36.4–36.6)	0.087
	Saturation (%)	94.0 (89.0–98.0)	96.0 (92.0–99.0)	0.004
	Respiratory Rate (/min)	24.0 (20.0–28.0)	24.0 (20.0–29.0)	0.962
Sex, Female (n(%))		80 (46.0)	58 (46.4)	0.942
Laboratory parameters	WBC (mcL)	11.8 (8.12–17.7)	11.0 (7.54–15.7)	0.264
	Neutrophils (/mm³)	10.22 (6.70–15.80)	8.97 (6.21–13.40)	0.170
	Lymphocytes (/mm³)	0.62 (0.38–1.02)	0.82 (0.54–1.13)	0.005
	Platelet (/mm³)	219.5 (141.0–299.0)	221.0 (177.0–292.0)	0.238
	CRP (mg/L)	108.0 (54.9–181.0)	95.0 (29.4–168.1)	0.235
	Procalcitonin (ng/mL)	1.13 (0.46–4.12)	0.16 (0.10–0.30)	<0.001
	Albumin (g/L)	28 (23–31)	35 (32–38)	<0.001
	Procalcitonin/Albumin	0.42 (0.016–0.158)	0.004 (0.002–0.009)	<0.001
Proportions	NLR	16,87 (8.17–30.30)	11.55 (6.06–20.05)	0.002

SBP: Systolic Blood Pressure (mmHg)
DBP: Diastolic Blood Pressure
NLR: Neutrophil/Lymphocyte Ratio

Table 3. ROC analysis results for procalcitonin/albumin ratio in determining mortality

Parameter	Cut-off Value	Sensitivity	Specificity	Area under the curve (AUC)	95; 95% CI:		p
					Lower Bound	Upper Bound	
Procalcitonin/Albumin	0.010	87.4	77.6	0.876	0.835	0.916	<0.001
NLR	23.15	37.9	83.2	0.607	0.544	0.671	0.002

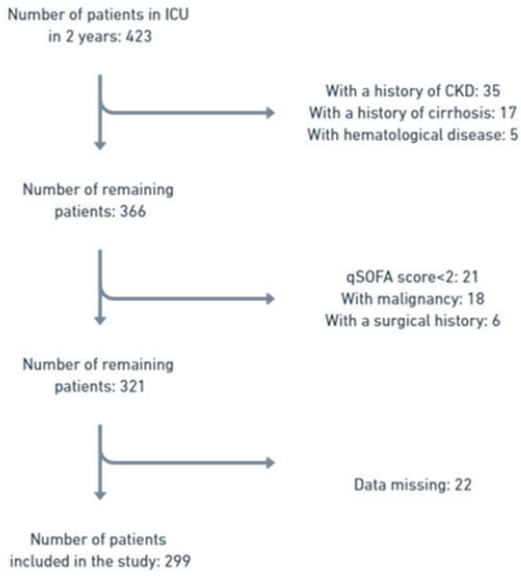

Figure 1. Flowchart of the cases included in the study

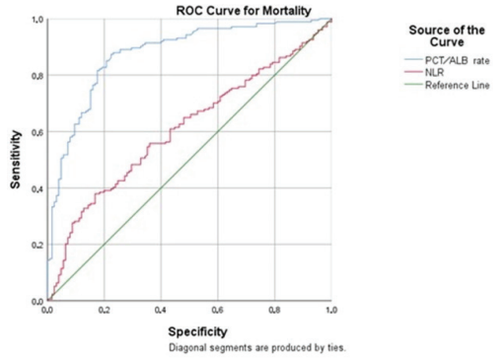

Figure 2. ROC analysis results of procalcitonin/albumin and NLR values for mortality

significantly higher in nonsurvivor patients (Table 2). The NLR rate was compared by the outcome of the cases. The results indicated that the NLR rate was significantly higher in nonsurvivor cases (Table 2).

A review of the results of the ROC analysis aimed to determine mortality by procalcitonin/albumin ratio indicated that the sensitivity and specificity of the procalcitonin/albumin ratio for a cut-off value of 0.010 were 87.4% and 77.6%, respectively, and the area under the curve (AUC) was 0.876. Upon analysis to test the success of the NLR value in predicting mortality, sensitivity and specificity were 37.9% and 83.2% for a cut-off value of 23.15, respectively, with an AUC of 0.607. In this context, upon review of the analyzed values the PAR was a promising parameter to use in determining mortality (Table 3 and Figure 2). The factors affecting mortality in the cases were analyzed and the effects of those factors were investigated. Upon univariate and multivariate regression analyses, decreases in albumin level and saturation had a significant effect on mortality. The factors, which increased the rate of mortality included decreased albumin level (OR = 1.148; 95% CI = 1.055–1.247; p = 0.001) and decreased saturation (OR = 1.240; 95% CI = 1.098–1.399; p = 0.001).

Discussion

Pneumosepsis is a disease associated with high rates of mortality due to multiorgan dysfunction induced by lung parenchymal involvement. Determining the prognosis of this disease can have an impact on the treatment process and mortality rate. Especially recently PAR finds use to determine prognosis in patients with sepsis [12]. To the best of our knowledge, there was no previous study in the relevant literature on applying PAR to determine the prognosis of patients diagnosed with adult pneumosepsis. In the present study, the sensitivity and specificity rates of PAR at ICU admission as an indicator of mortality in pneumosepsis patients were 87.4% and 77.6%, respectively.

In this study, the median age of patients diagnosed with pneumosepsis was 66.0 years (57.0–76.0). Of the 299 patients included in the study, 53.8% were men and 41.8% were discharged. In a study with 590 patients, 60.6% were men and the mean age was 65.6 ± 14.9 years [13]. Another study reported the mortality rate as 41.9% [12]. The age, sex, and mortality rates in our study are similar to the previous studies in the relevant literature. The fact that the most important reason for the progression of pneumonia to sepsis is advanced age and decreased lung capacity may account for this similarity.

In the present study, there was a significant difference between the survivor and nonsurvivor patient groups by age, systolic blood pressure (SBP), and saturation values at ICU admission. Similarly, a study by Çekiç et al. reported that the mean age of the nonsurvivors compared to the survivors [13]. This may be due to the fact that elderly patients are more susceptible to sepsis. A retrospective study by Boonmee et al., reported that SDB was significant as an indicator of mortality [14]. Another study found a significant difference between survivor and nonsurvivor patients with sepsis using SBP [15]. This might be associated with the impairment of vascular permeability due to sepsis. There was no previous study reported on saturation. This might be due to the fact that lung involvement was more prevalent in the nonsurvivor group.

PCT demonstrates higher specificity in bacterial infections compared to other proinflammatory markers [16]. Another study suggested that PCT was important for confirming the prognosis of bacterial sepsis [17]. Another study found that PCT was a better indicator than CRP in bacterial infections [18]. Although hypoalbuminemia in community-acquired pneumonia is a predictor of mortality, it has been reported to be an indicator of the severity of sepsis of abdominal origin but not significant as a predictor of mortality [19]. In addition, many previous studies confirmed that PCT and ALB were associated with the prognosis of sepsis [20]. In the present study, PCT was significantly higher and ALB was significantly lower in the nonsurvivor group. This may be due to the rapid spread of pneumosepsis in geriatric patients with an aggressive progression and that albumin is a negative acute phase reactant.

PAR assesses the infective and nutritional statuses. This increases its value in predicting prognosis in patients with pneumosepsis. A study on patients with acute respiratory distress syndrome suggested that PAR could be used as an independent predictor of 28-day mortality [21]. Consistently, Luo et al. suggested that PAR was an early predictor in patients with sepsis [22]. Another study, reported that PAR was higher in the nonsurvivor group [12]. PAR was confirmed as

an important predictor of 28-day mortality in a study of 128 adult patients with sepsis [23]. In the present study, consistent with the relevant literature, PAR in the nonsurvivor group was significantly higher compared to the survivor patients. This may be especially due to the combination of early elevation of PCT in bacterial infections and nutritional imbalance as a result of increased catabolism in sepsis.

In the present study, the sensitivity and specificity values of PAR as a predictor of mortality in patients with pneumosepsis with a cut-off value of 0.01 were 87.4% and 77.6%, respectively. Cekiç et al. reported that PAR had a cut-off value of 0.008 in patients with sepsis and it had a sensitivity of 70.7% and a specificity of 70.6% as a predictor of mortality [13]. Li et al. showed that the cut-off value of PAR as a mortality predictor was 0.256 with a sensitivity of 43.1% and a specificity of 81.5% in a study on patients with sepsis [12]. For the present study, we suggest that high PAR may be used as a predictor of mortality, especially in patients with severe sepsis, including pneumosepsis.

Limitation

There are some limitations associated with the present study. The most important limitation was that the study was designed as a retrospective, single-center research. Another limitation was the comparatively limited size of the sample. Therefore, future prospective and multicenter studies with a larger sample group will contribute to a better understanding of the issue.

Conclusion

Procalcitonin/albumin ratio can be used to determine the prognosis of patients, who are admitted to the ICU with a diagnosis of pneumosepsis as an easy, inexpensive, and rapid parameter. Therefore, pneumosepsis treatment can be started earlier and the mortality rate can be reduced.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or compareable ethical standards.

Funding: *None*

Conflict of Interest

The authors declare that there is no conflict of interest.

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How to cite this article:

Ertuğrul Altuğ, Doğanay Can, Adem Çakır, Kemal Şener, Mücahit Kapcı, Ramazan Güven. *An investigation of procalcitonin/albumin ratio as a predictor of mortality in patients with sepsis. Ann Clin Anal Med 2024;15(6):444-448*

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